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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,594	12/13/2005	Antonius Johannes Hendrikus Stegmann	2001-1418	7185

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EXAMINER	
BLUMEL, BENJAMIN P	
ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,594	STEGMANN ET AL.	
	Examiner	Art Unit	
	BENJAMIN P. BLUMEL	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,7-12,14,15,17,19 and 21-24* is/are pending in the application.

4a) Of the above claim(s) *11, 12 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4, 5, 7-10, 14, 15, 17, 19 and 21-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *November 18, 2008* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/18/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants are informed that the rejections of the previous Office action not stated below have been withdrawn from consideration in view of the Applicant's arguments and/or amendments.

Claims 1, 2, 4, 5, 7-10, 14, 15, 17, 19, 21-23 are examined on the merits. Claims 22 and 23 are new claims with new limitations. Furthermore, upon further consideration, the species election of group **(A-I)** has been withdrawn.

Election/Restrictions

This application contains claims 11, 12 and 24 are drawn to species nonelected without traverse in the reply filed on January 4, 2008.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on November 18, 2008 was filed after the mailing date of the non-final Office action on August 18, 2008. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Response to Amendment

The declaration under 37 CFR 1.132 filed November 18, 2008 is sufficient to overcome the rejection of claims 1-5 and 14-18 based upon 35 U.S.C. 103(a) for the Stegmann publication not being by another.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

> the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

(New Rejection Necessitated by Amendments) Claims 1, 2, 4, 5, 7-10, 14, 15, 17, 19 and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zurbriggen et al. (Progress in Lipid Research, 2000), Cullis et al. (US Pat. 6,417,326 B1), Gluck and Metcalfe (Vaccine, 2003) and Jira and Jirathitikal (US PGPub 2003/0092145 A1).

The claimed invention is drawn to a pharmaceutical composition of a reconstituted viral membrane, the lipid bilayer comprising natural lipids of a viral membrane of which comprises a fusion protein of a virus, an amphiphilic adjuvant and, optionally, a further antigen, whereby:

(a) the lipid bilayer has a lipid composition that is compatible with fusion, induced by the fusion protein, of the viral membrane with the membrane of a cell that can be fused with the virus from which the fusion protein is derived;

(b) the fusion protein and the amphiphilic adjuvant interact with the hydrophobic interior of the lipid bilayer; and,

(c) the fusion protein, the amphiphilic adjuvant and the optional further antigen are not covalently linked. The amphiphilic adjuvant is the lipopeptide (N-palmitoyl-S-2,3(bisoleoyloxy)-propyl-cysteinyl-seryl-serine) and is also a ligand for a mammalian (TLR) Toll-Like Receptor. This composition is suitable for intranasal, oral or parenteral administration. The viral fusion protein used is that of an integral membrane protein, such as the viral antigen hemagglutinin (HA) of influenza viruses. While the new claims requires the viral fusion protein be hemagglutinin and the further antigen by

neuraminidase, independent claim requires that the further antigen by an optional limitation for the instant invention. Therefore, any teaching of neuraminidase is not required.

Zurbriggen et al. teach a reconstituted influenza virosomes (IRIV) which contain lipids from influenza viral envelopes, and phosphatidylcholine (PC) and phosphatidylethanolamine (PE). The IRIV also contained influenza cell fusion protein hemagglutinin (HA), which traverses the bilayer and interacts with interior vesicle of the IRIV. The PE and PC also provide an adjuvant effect as part of the viral envelope, while interacting with both the inside and outside of the virosome. The virosome compositions discussed by Zurbriggen et al. are designed for *in vivo* use in order to induce effective B and T cell immune responses. However, Zurbriggen et al. do not teach the specific adjuvant/lipopeptide of N-palmitoyl-S-2,3 (bispalmitoyloxy)-propyl-cysteinyl-seryl-serine; *See pages 3-6.*

Cullis et al. teach the formation of virosome-liposome fusion molecules which allows for the transportation of large therapeutic molecules to target cells. In order to do this, Cullis et al. encapsulate that therapeutic compound with a liposome, which is made up of lipopeptides. The virosome containing influenza HA proteins is then fused with the liposome. *See columns 3, 16, 31 and 32.*

Gluck and Metcalfe teach the use of immunopotentiating reconstituted influenza virosomes (IRIVs), an empty bilayer molecule with contain intercalated influenza HA and NA on its surface. Gluck and Metcalfe discuss the adjuvant properties of IRIVs and their ability to target specific cells and fuse with them. Furthermore, when these IRIVs

are administered with an adjuvant, a strong localized and systemic immune response is induced when administered intranasally. *See pages 611 and 614.*

Jira and Jirathitikal suggest that formation of immunogenic compositions based on viruses and/or viral antigens along with adjuvants, such as N-palmitoyl-S-2,3 (bispalmitoyloxy)-propyl-cysteinyl-seryl-serine. *See paragraphs 18, 22, 81, 98 and 101.*

It would have been obvious to one of ordinary skill in the art to modify the composition taught by Zurbriggen et al. in order to used virosomes, instead of co-micelles in presenting viral fusion proteins and lipoprotein adjuvant N-palmitoyl-S-2,3 (bispalmitoyloxy)-propyl-cysteinyl-seryl-serine. One would have been motivated to do so, given the suggestion by Zurbriggen et al. that the a virosome can also present viral fusion proteins along with other proteins and some of the components of IRIVs posses adjuvant type properties. There would have been a reasonable expectation of success, given the knowledge that lipopeptide comprosing liposomes can be fused to virosomes in order to transmit larger therapeutic products, as taught by Cullis et al., also given the knowledge that adding an external adjuvant to the IRIV enhances immune responses, as taught by Gluck and Metcalfe and also given the knowledge that Jira and Jirathitikal teach the use of the adjuvant N-palmitoyl-S-2,3 (bispalmitoyloxy)-propyl-cysteinyl-seryl-serine for use with immunogenic compositions. Thus the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BENJAMIN P. BLUMEL whose telephone number is (571)272-4960. The examiner can normally be reached on M-F, 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-1600. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Stacy B Chen/
Primary Examiner, Art Unit 1648

/BENJAMIN P BLUMEL/
Examiner
Art Unit 1648